REMARKS/ARGUMENTS

Claims 1 and 13 have been revised to correspond to the Restriction Requirement mailed September 21, 2006 and Applicants' election. Applicants expressly reserve the right to re-present, without prejudice, claims encompassing the removed subject matter in a continuing application. Claims 1 and 13 have also been revised to include the feature of oligonucleotide length, which was inherently within the scope of the claims as previously presented. Support for the revision is provided at least on page 18, lines 1-5; and page 66, paragraph [00228] lines 1-3 therein, of the instant application.

Claim 11 has been revised to be directed to a disclosed aspect to the invention, which is supported at least on page 13, paragraph [0084], of the instant application.

Claim 12 has been revised so that it directly depends from claim 1.

No new matter has been introduced, and entry of the above revised claims is respectfully requested.

Alleged issues under 35 U.S.C. § 112, first paragraph

Claims 1, 6-8, and 29-31 were rejected under 35 U.S.C. § 112, first paragraph as allegedly "failing to comply with the written description requirement." Applicants have carefully reviewed the statement of the rejection and respectfully traverse because no *prima facie* case of an inadequate written description has been presented.

As an initial matter, Applicants point out that there are only claims 1-22 pending in the instant application. Therefore, the rejection of claims "29-31" by the instant rejection is not understood. Additionally, the discussion of nematodes on page 3 of the Office Action mailed January 4, 2007 is not understood because it appears irrelevant to the instant application.

Additionally, Applicants note that pending claims 2-5 and 9-22 were not rejected by the instant rejection, and so no allegation of an inadequate written description has been raised with respect to those claims.

Turning to the content of the instant rejection, Applicants respectfully point out that the statements therein appear to reflect a misapprehension of the claimed invention. Applicants respectfully point out that claims 1 and 13, for example, feature a composition comprising two components, one of which is an oligonucleotide containing no CpG motifs and with a defined length. The rejection focuses on this component of the claims and alleges that there is an inadequate representation of "the numerous ribonucleotides, deoxyribonucleotides, or chemically modified oligonucleotides of any size or sequence composition, lacking CpG motifs" to support the genus of oligonucleotides that may be used within the scope of the claims.

But the above quote clearly shows that there is a misunderstanding of what is necessary in the form of representative examples. Applicants respectfully point out that a skilled person would clearly understand the oligonucleotide to be one which contains any sequence as long as it does not contain a CpG dinucleotide (where the "p" in CpG simply represents a phosphate moiety present between the cytosine and guanine residues). So in the case of a DNA oligonucleotide containing only adenine (A), thymidine (T), guanine (G), and cytosine (C) residues as an example, the oligonucleotide may contain any of the other 15 possible dinucleotides which are clearly known to the skilled person. Stated differently, the skilled person would understand that a DNA oligonucleotide as featured in claims 1 and 13 may contain any of the following 15 non-CpG dinucleotide sequences:

AA, AT, AG, AC, TA, TT, TG, TC, GA, GT, GG, GC, CA, CT, and CC.

Therefore, and contrary to the statement of the rejection, these non-CpG dinucleotide sequences are the structural features, or specific characteristics, which define the oligonucleotides of the claimed invention. Given these structural characteristics, the oligonucleotides featured in the claims are clearly not described only by a functional characteristic as alleged in the statement of the rejection.

In light of the above, Applicants point out that an adequate description of the claimed subject matter may be met by simply describing oligonucleotides containing representative examples of non-CpG dinucleotide sequences, where the oligonucleotides produce a systemic, non-antigen-specific immune response when used with a liposome delivery vehicle as recited in the claims. The instant application provides representative examples of these

dinucleotide sequences as shown in Examples 12-15. For example, the oligonucleotides represented by SEQ ID NOs:2 and 3 contain the following dinucleotide sequences:

AT, AG, AC, TA, TG, TC, GA, GT, GG, CA, and CT in SEQ ID NO:2; and

AT, AG, AC, TA, TT, TG, TC, GA, GT, CA, and CT in SEQ ID NO:3.

The oligonucleotides represented by SEQ ID NOs:4 and 5 contain additional combinations of these non-CpG dinucleotide sequences.

As described in the examples, the oligonucleotides represented by SEQ ID NOs:2-5 all produce the immune response as featured in the claims when used with a liposome delivery vehicle as recited in the pending claims. This is shown by the data in Figures 30-33. So given the multiple occurrences of the non-CpG dinucleotide sequences within the oligonucleotides used in Examples 12-15, it is clearly evident that the presence of these sequences in an oligonucleotide, when used with a liposome delivery vehicle, elicits the featured immune response.

Because the claims are directed to oligonucleotides containing these 15 non-CpG dinucleotide sequences, a skilled person provided with Examples 12-15 and Figures 30-33 of the instant application would clearly understand that there is a representative, and adequate, description of the non-CpG dinucleotide sequences as present in the oligonucleotides encompassed by the pending claims. Therefore, and contrary to the assertion in the instant rejection, there is no requirement for additional representatives of the claimed invention.

To further support the above, Applicants respectfully submit that there is ample precedent for even a single representative species to adequately support a genus. For example, and as discussed at MPEP 2163IIA.3.(a)ii),

> there may be situations where one species adequately supports a genus. See, e.g., *Rasmussen*, 650 F.2d at 1214, 211 USPQ at 326-27 (disclosure of a single method of adheringly applying one layer to another was sufficient to support a generic claim to "adheringly applying" because one skilled in the art reading the specification would understand that it is unimportant how the layers are adhered, so long as they are adhered); *In re Herschler*, 591 F.2d 693, 697, 200 USPQ 711, 714 (CCPA 1979) (disclosure of corticosteroid in DMSO sufficient to support claims drawn to a method of using a mixture of a "physiologically active steroid" and DMSO because "use of known chemical compounds in a manner auxiliary

> to the invention must have a corresponding written description only so specific as to lead one having ordinary skill in the art to that class of compounds. Occasionally, a functional recitation of those known compounds in the specification may be sufficient as that description."); *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 285 (CCPA 1973) (the phrase "air or other gas which is inert to the liquid" was sufficient to support a claim to "inert fluid media" because the description of the properties and functions of the air or other gas segmentizing medium would suggest to a person skilled in the art that appellant's invention includes the use of "inert fluid" broadly.)

Given the legal precedent for even a single species to support claims to a genus of embodiments, the description of multiple examples of non-CpG dinucleotide sequences in the disclosed oligonucleotides is more than sufficient to provide an adequate written description.

With respect to the alleged issue regarding "ribonucleotides" in the statement of the rejection, Applicants point out that ribonucleotides merely introduce the possibility of a uracil (U) residue (in place of thymidine) into the set of non-CpG dinucleotide sequences as follows:

AA, AU, AG, AC, UA, UU, UG, UC, GA, GU, GG, GC, CA, CU, and CC.

This merely introduces an addition of 7 possible uracil containing dinucleotide sequences to the 15 described above for a total of 22 sequences. But even with a total of 22 possibilities, the disclosed oligonucleotides exemplify more than 55% of the 22 dinucleotide possibilities. If even a single species may be sufficient to support a genus, Applicants respectfully submit that there is no demonstration that exemplification of over 55% of the possible non-CpG dinucleotides is insufficient to support the pending claims.

Finally, and with respect to the alleged issue regarding "chemically modified oligonucleotides of any size" in the statement of the rejection, Applicants respectfully point out that the claims now feature a specific size range for the oligonucleotides. Moreover, the allegation regarding "chemically modified oligonucleotides" is misplaced because there is no basis to require an adequate written description of a "chemically modified oligonucleotide" when the claims are not limited by such a feature. To the contrary, all that is needed is a written description of the invention, which features "an oligonucleotide containing no CpG motifs".

In light of the significant description the dinucleotide sequences which structurally define the oligonucleotides recited in the claims, Applicants respectfully submit that no *prima facie* case of an inadequate written description is present. The instant rejection is misplaced and may be properly withdrawn.

Claims 1-22 were rejected under 35 U.S.C. § 112, first paragraph as allegedly "failing to comply with the enablement requirement." Applicants have carefully reviewed the statement of the rejection and respectfully traverse because no *prima facie* case of non-enablement has been presented.

As an initial matter, Applicants point out that the standard to apply in establishing a *prima facie* case of non-enablement is set out in part at MPEP 2164.04 and by the cases cited therein, including the guidance provided by *In re Marzocchi*.[1] With reference to *Marzocchi*, the standard states in part that

> "A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. § 112, first paragraph, unless there is a reason to doubt the *objective* truth of the statements contained therein which must be relied on for enabling support." (underlining and italics added)

Therefore, and contrary to the instant statement of the rejection, there is a presumption of enablement such that the burden is on the part of the Office to provide *objective* reasons to defeat the presumption. Mere reliance on assertions of possibilities or conjectures are not enough. There must be objective reasons why undue experimentation is necessary to make and use the claimed invention.

Moreover, Applicants respectfully point out that undue experimentation is not the same as the absence of experimentation. To the contrary, the presence or need for routine and

[1] 439 F.2d 220, 169 USPQ 367 (CCPA 1971).

repetitive experimentation, like that involved in the facts of *In re Wands*[2], is entirely consistent with the presence of an enabling disclosure and so contrary to an assertion of non-enablement.

In the instant application, the disclosure, and thus claims, were enabling as originally filed for the full scope of the claims because no adequate and objective reasons are present to doubt the ability to make and use a composition comprising a liposome delivery vehicle and an oligonucleotide containing no CpG motifs (and from more than 10 to about 500 nucleotides in length) where the composition elicits a systemic, non-antigen-specific immune response when administered to a mammal. Applicants point out that statement of the rejection appears to erroneously focus on "a treatment of tumors in a mammal", which is not a limitation of any pending claim. So while eliciting a systemic, non-antigen-specific immune response in a mammal with a composition of the invention may include the generation of an immune response that is beneficial in the treatment of tumors in the mammal, there is no basis to require specific enablement of "treating tumors" when the claims do not recite such a limitation. To the contrary, the focus must remain on the presumption of enablement for a composition that elicits a systemic, non-antigen-specific immune response.

Contrary to the instant rejection, the application as filed provides guidance and working examples of compositions that elicit a systemic, non-antigen-specific immune response. This is acknowledged on page 6 of the Office Action mailed January 4, 2007, which includes the statement that "Examples 12-15 of the instant specification are provided to demonstrate the potential therapeutic effects of oligonucleotides lacking CpG motifs, in eliciting a systemic, non-antigen specific immune response in a mammal." Given such evidence, the statement of the rejection erroneously attempts to shift the focus from the immune response recited in the claims to the issue of "reducing tumor size in a mammal." Applicants respectfully submit that the shift does not support the allegation of non-enablement because the claims are not directed to "reducing tumor size".

Additionally, Applicants point out that the conjectures regarding Examples 12, 14, and 15 as presented on pages 6-7 are inappropriate. There is no room for the allegations of

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2 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988).

possible alternative interpretations or possibilities as somehow supporting an allegation of non-enablement because *the presumption of enablement means that the Examples must be taken as supporting enablement*. Simply put, and as long as the Examples are consistent with the claimed invention as presented by Applicants, *Marzocchi* requires that *the Examples be presumed to support enablement*. So the Examples cannot be attacked or used against the Applicants unless there is an objective reason to doubt the support provided by the Examples.

Applicants point out that Examples 12-15 are all consistent with the invention in that oligonucleotides lacking a CpG motif, and of a length of more than 10 to about 500 nucleotides, have activities that correspond to eliciting a systemic, non-antigen-specific immune response when used in combination with a liposome delivery vehicle. The observation that an oligonucleotide containing a CpG motif has similar T and B cell activating properties is irrelevant to the scope of the claims, which excludes a CpG containing oligonucleotide.

Furthermore, the two additional documents cited in the statement of the rejection do not support the allegation of non-enablement. The Auf et al. document reports results with oligonucleotides *in the absence of* a liposome delivery vehicle. Therefore, the observations described therein do not support the allegation of non-enablement. Similarly, the Vollmer et al. document also only reports results observed with oligonucleotides *in the absence of* a liposome delivery vehicle. Therefore, allegations based upon Vollmer et al.'s comparisons of CpG containing and CpG lacking oligonucleotides do not support the instant rejection because they cannot account for the presence of a liposome delivery vehicle as recited in the claims. Moreover, Vollmer et al's description of a "new" sequence motif that has immune stimulatory activity does not negatively affect enablement for the claimed invention. To the contrary, the "new" motif is consistent with the instant invention in that the "new" motif also lacks a CpG motif. Therefore, and contrary to the statement of the rejection, Vollmer et al.'s "new" motif should support enablement for the claimed invention because it would be expected to elicit a systemic, non-antigen specific immune response when used with a liposome delivery vehicle.

In light of the above, Applicants respectfully submit that no objective basis for the lack of enablement has been presented. There is no evidence that undue experimentation would

be needed to make and use compositions as encompassed by the scope of the claims. The skilled person is knowledgeable with respect to oligonucleotide production, including the preparation of CpG lacking oligonucleotides. And there is no demonstration of undue experimentation in combining a CpG lacking oligonucleotide with a liposome delivery vehicle to form a composition for administration to a mammal to elicit a systemic, non-antigen specific immune response as disclosed by the instant application.

Given the lack of undue experimentation to make and use composition as claimed, Applicants respectfully submit that no *prima facie* case of non-enablement is present. The instant rejection is thus misplaced and may be properly withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 858-350-6100.

Respectfully submitted,

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